UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,685	04/03/2002	Patricia Anne Nuttall	2488-1-002	6308

23565 7590 03/24/2005

KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 03/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,685	NUTTALL ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 January 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *8,9,16,17,44-50 and 52-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *52* is/are allowed.

6)☒ Claim(s) *8,9, 16,17, 44-50 and 53-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 01/26/05 is acknowledged.

Claims 8-9, 16-17, 44-50 and 52-54 are pending.

Claims 8-9, 16-17, 44-50 and 52-54 read on a recombinant protein derived from a blood-feeding arthropod ectoparasite that inhibits tryptase and a pharmaceutical composition comprising said protein a vaccine comprising said protein and a process for the formulation of a pharmaceutical composition comprising said protein under consideration in the instant application.

In view of the amendment, filed 01/26/05 the following rejection remains:

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-9, 16-17, 45-50 and 53-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an the protease inhibitor protein of SEQ ID NO:2, derived from tick *R. appendiculatus* and active fragment of said protein that inhibits tryptase with Ki of less than $1x10^{-6}$ M does not reasonably provide enablement for : (i) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, 90% or 95 % of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claim 8-9 , 45-49, and 53-54 or (ii) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO: that has been genetically or chemically fused to one or more peptides, or bound to a support, such as resin , as claimed in claims 16 and 17; or (v) any anti-tryptase agent comprising any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease

inhibitor, wherein said homology is 80% of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claims 50 .

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, 09/22/04

Applicant's arguments, filed 01/26/05 have been fully considered, but have not been found convincing.

Applicant asserts that ; (i) generating active fragments of SEQ ID NO:2 would be well within the capabilities of an ordinarily skilled artisan; (ii) the specification is enabled for a recombinant protein derived from a blood-feeding arthropod and exhibits sequence homology 80 % or more with sequence of SEQ ID NO:2. (iii) The Specification teaches the skilled person how to determine whether a candidate protein meets the sequence requirements.

Contrary to Applicant's assertion, the issue raised in the previous Office Action was not about ability of one skill in the art to generating an active fragment of TdPI of SEQ ID NO:2, that inhibits tryptase.

In the previous Office Action it was stated that Applicant discloses a protease inhibitor protein sequence of SEQ ID NO:2, derived from tick *R. appendiculatus* which inhibits tryptase (see page 10 and Fig. 1 in particular).

Applicant has not taught how to make and/or use (i) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, 90% or 95 % of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claim 8-9 , 45-49, and 53-54 or (ii) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO: that has been genetically or chemically fused to one or more peptides, or bound to a support, such as resin , as claimed in claims 16 and 17; or (v) any anti-tryptase agent comprising any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80% of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claims 50. The structural and functional characteristics of said recombinant protein derived from blood-feeding arthropod

ectoparasite or from tick, that inhibits tryptase or active fragment of said protein or functional equivalent of said protein are not defined in the claim.

Since the instant fact pattern fails to indicate that representative number of structurally related compounds is disclosed, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claims and consequently would not know how to make them. An assay for *finding* a product is not equivalent to a positive recitation of *how to make* a product.

Applicant is relying upon certain biological activities and the disclosure of a single species to support an entire genus. It is well known that minor structural differences among even structurally related compounds or compositions can result in substantially different biology, expression, and pharmacology of proteins. Therefore, structurally unrelated: (i) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, 90% or 95 % of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claim 8-9 , 45-49, and 53-54 or (ii) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO: that has been genetically or chemically fused to one or more peptides, or bound to a support, such as resin , as claimed in claims 16 and 17; or (v) any anti-tryptase agent comprising any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80% of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claims 50 would be expected to have greater differences in their activities.

The references cited in the previous Office Action demonstrated that even a single amino acid substitution or modification can often dramatically affect the biological activity and characteristic of a protein. Thus, in view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:2* to *share the same function* as the polypeptide of SEQ ID NO:2.

Without sufficient guidance, the changes which can be made in the structure of: (i) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, 90% or 95 % of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claim 8-9 , 45-49, and 53-54 or (ii) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment

of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO: that has been genetically or chemically fused to one or more peptides, or bound to a support, such as resin , as claimed in claims 16 and 17; or (v) any anti-tryptase agent comprising any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80% of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claims 50 and still maintained the function of tick-derived protease of SEQ ID NO:2, derived from tick *R. appendiculatus* is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, 90% or 95 % of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claim 8-9 , 45-49, and 53-54 or (ii) any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80%, of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO: that has been genetically or chemically fused to one or more peptides, or bound to a support, such as resin , as claimed in claims 16 and 17; or (v) any anti-tryptase agent comprising any recombinant protein derived from blood-feeding arthropod ectoparasite or from tick or any active fragment of said protein , that inhibits tryptase and wherein said protein exhibits significant sequence homology with the tick-derived protease inhibitor, wherein said homology is 80% of the amino acid of the tick-derived protease inhibitor protein set forth in SEQ ID NO:2, as claimed in claims 50 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

The following new grounds of rejection is necessitated by the amendment filed 01/26/05

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 44 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 44 is indefinite and ambiguous in the recitation of " a recombinant protein or protein fragment comprising the TdPI sequence of SEQ ID NO:2." The specification disclosed that SEQ ID NO:2 is a full length TdPI. It is unclear how a fragment of the protein can comprise the full length protein?

5. The prior art does not teach or suggest a recombinant protein comprising SEQ ID NO:2 or a protein fragment thereof, as recited in claim 52.

6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
March 14, 2005

Christina Chan

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600